

Remarks/Arguments

Reconsideration of the application in view of the current amendments of November 4, 2002, and following remarks is respectfully requested.

Claims 2 - 63 and 197 remain pending in this application.

Amendment to Claim 197

Claim 197 has been amended to add the word "modified" into the claim elements as well as in the preamble of the claim. The amendment is made without prejudice or disclaimer to the subject matter contained therein. Support for the amendment can be found in the Specification. No new matter has been added.

Rejections under 35 U.S.C. § 103(a)

In the Office action, claims 2 - 63, and 197 were rejected under 35 U.S.C. §103 as being unpatentable over Malfroy-Camine et al., in view of Burt et al.

Specifically, the Office action asserts that Malfroy-Camine et al., disclose "a synthetic catalytic free radical scavenger useful as antioxidants for prevention and therapy of disease. The catalyst is a non proteinaceous material having manganese and iron chelates compounds. Malfroy-Camine et al fails to disclose the use of the catalysts in combination with a substrate or carrier. Burt et al teaches synthetic free radical scavenger that are used to reduce tissue damage. Burt, et al, column 11, teaches that the catalysts may be used with a substrate or a carrier including biomaterials. To provide the catalysts of Malfroy-Camine et al with a biomaterial substrate or carrier to more effectively control the rate of release during the administering of the catalysts at the specific tissue site would have been obvious from the teachings of Burt et al."

The Office action also asserts that

" ... in light of the teachings of Burt, et al the combination of a catalysts to a substrate or a carrier would have led on(sic) with ordinary skill in the art to provide a means for controlling the location of the catalysts as well as tailored regulation of the catalysts in vivo."

Applicants respectfully traverse. Applicants submit that the Office action has failed to state a *prima facie* case for obviousness. The burden of proof in establishing a *prima facie* case of obviousness under § 103 rests with the Patent Office. *In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir.1984). In establishing a *prima facie* case, the Patent Office, among other things, must show that (1) the prior art would have suggested to those of ordinary skill in the art that they should make the claimed invention and (2) that the prior art would have revealed a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1999). In addition, the prior art reference (or references when combined) must teach or suggest all the claim limitations. "Both the suggestion and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure." *Id.*, see also MPEP § 2143. Thus, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). "the factual inquiry whether to combine references must be thorough and searching. It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with." *In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (citations omitted).

The present Office action fails to provide objective evidence of *any* suggestion or motivation in the prior art to combine and modify the cited references. Instead, the Office action merely states that such combination and modification "would have obvious from the teachings" It is now well-

established that "[b]road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence'." *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999); see also *In re Kotzab*, 217 F.3d at 1370. "Th[e] factual question of motivation is material to patentability, and [can] not be resolved on subjective belief and unknown authority." *In re Lee*, 277 F.3d at 1343-1344. Because the Office action fails to provide any objective evidence from the prior art of a motivation to modify and combine the cited references along with a reasonable expectation of success, Applicants respectfully submit that the Office action fails to state a *prima facie* case of obviousness but rather relies upon hindsight in combining the various disparate references in contravention of the Federal Circuit's ruling in *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566 (Fed. Cir. 1996).

Additionally Applicants respectfully submit that the Office has failed in its burden to show that when the invention is considered *as a whole* and the references are considered as a whole, as required by law, that the prior art references teach or suggest all the claim limitations of applicants invention.

The Office action admits that Malfroy-Camine et al fail to disclose the use of the catalysts in combination with a substrate or carrier. Burt et al., disclose imidazole derivatives that may be combined with a *carrier* (see, Claims 46 and 47, and col. 11, lines 16, 19, 23, 25, 30, 35, 37, and 42), which may be a biomaterial such as a liposome (Col. 11, line 12) or delivery device (Claim 47). Burt et al. do not disclose a substrate, as described in the present application. When Burt et al., is taken *as a whole* the reference teaches a compound to be released from the carrier, delivery device or biomaterial. Applicants specifically disclose that "the term 'biomaterial' is not meant to encompass drugs and biologically active molecules such as ... lipids ..."¹. Applicants do not disclose a

¹ Page 9 of the application: As used herein, the term "biomaterial" is not meant to encompass drugs and biologically active molecules such as steroids, di-saccharides and short chain polysaccharides, fatty acids,

carrier anywhere. Taken as a whole, Applicants disclose a modified biomaterial, where "modification" means there is physical association between the biomaterial and catalyst or precursor ligand, whereby it becomes integrated into or onto the biomaterial². The reference of Burt et al. teaches away from the invention of Applicants and therefore does not suggest or motivate the present invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)

The Office action's assertion that

"in light of the teachings of Burt, et al. the combination of a catalysts to a substrate or carrier would have led on with ordinary skill in the art to provide a means for controlling the location of the catalysts as well as tailored regulation of the catalysts in vivo"

fails to consider the reference of Burt et al., in its *entirety*. 35 U.S.C. §103, and MPEP § 2141.02. . "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). The Office action's same assertion also impermissibly distills the invention down to a "gist" or a "thrust" and disregards the "as a whole" requirement. See 35 U.S.C. §103 and MPEP §2124.02. "Distilling an invention down to the "gist" or "thrust" of an invention disregards the requirement of analyzing the subject matter "as a whole." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)

There is no motivation or suggestion within the references to combine

amino acids, antibodies, vitamins, lipids, phospholipids, phosphates, phosphonates, nucleic acids, enzymes, enzyme substrates, enzyme inhibitors, or enzyme receptor substrates.

Malfroy-Camine et al., and Burt et al. There is no reasonable expectation of success if the references are combined, as Burt et al., taken as a whole teaches away from Applicants invention.

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious. This court has previously stated that '[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'

In re Fritch, 972 F.2d 1260, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992).

Applicants respectfully submit that current rejections function exactly in the manner the court in *In re Fritch* warns against. The rejections impermissibly cite different features of the claimed invention from a prior art source without the motivation or suggestion in the art to modify the reference. "[The] Examiner must prove that it would have been obvious to modify the references, without having access to the application under examination to arrive at the claimed invention." *Lear Siegler, Inc. v. Aeroquip Corp.*, 733 F.2d 881, 221 USPQ 1025, 1033 (Fed. Cir. 1984).

With regard to the Office action statement

"in light of the teachings of Burt, et al the combination of a catalysts to a substrate or carrier would have led on with ordinary skill in the art to provide a means for controlling the location of the catalysts as well as tailored regulation of the catalysts in vivo"
(page 2-3 of the Office Action)

the Office action does not provide evidence to support the statement. Applicants respectfully traverse the assertion and request that the rejection be withdrawn or

² Page 10 of the application: "modification" means any method by which a physical association may be effected between a biomaterial and a non-proteinaceous catalyst for the dismutation of superoxide, whereby the non-proteinaceous catalyst becomes integrated into or onto the biomaterial.

that an affidavit be provided from Examiner in support of the statement, as required of Examiner pursuant to 37 C.F.R. §1.104(d)(2) and MPEP §2144.03.

MPEP §2144.03 states that

"If applicant does not seasonably traverse the well known statement during examination, then the object of the well known statement is taken to be admitted prior art. *In re Chevenard*, 139 F.2d 71, 60 USPQ 239 (CCPA 1943). A seasonable challenge constitutes a demand for evidence made as soon as practicable during prosecution. Thus, applicant is charged with rebutting the well known statement in the next reply after the Office action in which the well known statement was made.

Applicants arguments above point out that Applicants do not consider Burt et al. to be admitted prior art or to teach or suggest any part of Applicants invention.

In addition to the points made above, it should be emphasized that Burt et al. do not teach or suggest the use of a *non-proteinaceous catalyst for the dismutation of superoxide*, even attached to a carrier for release, much less immobilized on a biomaterial for ongoing catalysis for dismutation of superoxide anions. See, e.g., *Burt et al.*, at col. 4, l. 9 et seq., col. 6, l. 28 et seq. As stated in Applicants application, "[p]rior to applicants' invention, *it was not known* that non-proteinaceous catalysts for the dismutation of superoxide could be *immobilized* on the surface of a biomaterial and still retain their catalytic function and exhibit an anti-inflammatory effect." Accordingly, the rejection should be withdrawn.

Rejections under 35 U.S.C. § 102(e), or in the alternative under 35 U.S.C. §103(a)

In the Office action, claim 197 was rejected under 35 U.S.C. §102(e) as being anticipated by, or in the alternative, under 35 U.S.C. §103(a) as obvious over Bush et al.

Specifically, the Office action asserts that Bush et al.,
“discloses the use of a metal chelating catalyst in combination with implant. It is not clear what form the implant possesses, however it is well known in the art to complex active molecules to a substrate or carrier designed for implanting. Such devices may include prosthetic type devices and drug release devices. In either instances, the substrate or carrier of the devices may be considered a biomaterial.”

Applicants respectfully traverse. Applicants submit that the Office action has failed to state a *prima facie* case for anticipation or obviousness. The requirements the Office must meet for a *prima facie* case apply with equal force with regard to the instant rejection and are expressly asserted here again in response to the Office’s rejections of Claim 197 under 35 U.S.C. § 102(e), or in the alternative under 35 U.S.C. § 103(a).

Bush et al. have a substantially different focus and do not anticipate or suggest Applicants’ claimed invention. Bush et al. teach the administration of metal chelating compounds that inhibit the metal-mediated production of superoxide in a stoichiometric fashion (see Bush et al., cols. 13-14, particularly col 13, ll. 25-30) by removing the chelated metals from a patient to prevent beta-amyloid production of ROS. Further, solely as a delivery mechanism, Bush et al. disclose that its therapeutic compounds may be administered “in any convenient manner . . . such as by . . . implant . . .” (Bush et al., col. 16, ll. 43-47). Clearly,

they do not contemplate or suggest attachment to a biomaterial to accomplish long-term catalysis of the dismutation of superoxides.

Thus, Bush et al. do not anticipate or make obvious the claimed invention due to their failure to teach or suggest any one or more of the following claimed elements:

- a modified biomaterial,
- a non-proteinaceous catalyst (or its precursor)
- wherein the catalyst/precursor is attached to the biomaterial, and
- wherein the catalyst is capable of dismutating superoxide (vs. removing metals involved in generating superoxides).

Hence, Bush et al., are far from identical to the present invention and Bush et al. do not teach or suggest all of the elements of Applicants' invention. Bush et al. teach methods of diminishing beta-amyloid ROS production by the chelation of metals captured in the beta-amyloid "zinc-finger" motif. The chelated metal is meant to be *removed* from a patient to prevent beta-amyloid production of ROS. Bush et al., teach different compounds from Applicants' to be administered to be released from a delivery vehicle such as an implant. In contrast, Applicants supply a metal-complexed catalytic compound, and disclose a modified biomaterial or implant, where "modification" means there is physical association between the biomaterial and catalyst or precursor ligand, whereby it becomes integrated into or onto the biomaterial.³ Although the word "implant" is found in both Bush et al., and the present application, taken in the proper internal context, the word has a different meaning in Bush et al., than it does as used by Applicants.

The Office action states in regard to Bush et al. as it relates to Applicants' invention that "it is well known in the art to complex active molecules to a

³ Page 10 of the application: "modification" means any method by which a physical association may be effected between a biomaterial and a non-proteinaceous catalyst for the dismutation of superoxide, whereby the non-proteinaceous catalyst becomes integrated into or onto the biomaterial.

substrate or carrier designed for implanting" (page 3 of the Office action). The Office action does not provide evidence to support the statement, or demonstrate its relationship to Long-term catalysis of the dismutation of superoxides.

Applicants respectfully traverse the assertion and request that the rejection be withdrawn or that an affidavit be provided from Examiner in support of the statement, as required of Examiner pursuant to 37 C.F.R. §1.104(d)(2) and MPEP §2144.03.

Applicants arguments above point out that Applicants do not consider Bush et al. to be admitted prior art or to teach or suggest any part of Applicants' invention. As stated in Applicants application, "[p]rior to applicants'invention; *it was not known* that non-proteinaceous catalysts for the dismutation of superoxide could be immobilized on the surface of a biomaterial and still retain their catalytic function and exhibit an anti-inflammatory effect."

CONCLUSION

In light of the foregoing remarks and amendment, Applicants respectfully request reconsideration and withdrawal of all final rejections set forth in the Office action of January 30, 2003. Further, Applicants respectfully submit that all claims presently under consideration are in a condition for allowance and request issuance of a Notice of Allowance at Examiner's earliest convenience.

Should the Examiner have any remaining questions regarding the subject invention or its patentability, Applicants encourage the Examiner to contact the undersigned to answer such questions or provide additional information

Respectfully submitted,

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